

LETTERS TO THE EDITOR

Stavudine induced macrocytosis

Recently we noted that patients on stavudine among our cohort of HIV positive patients were tending to have an elevated mean corpuscular volume (MCV). This prompted us to perform a retrospective analysis of the case notes of all our patients on stavudine ($n = 21$, 19 males, two females). Four patients were excluded from analysis: one patient had bone marrow failure of unknown origin and was transfusion dependent; one patient was found to have a low folate level secondary to HIV enteropathy; and two patients known to have very high alcohol intakes. The patient found to be folate deficient had only 4 weeks' treatment with stavudine during which time his MCV rose by $2.4 \times 10^{15}/l$. Both patients with a high alcohol intake showed increasing MCVs on stavudine: one of $5.3 \times 10^{15}/l$ over 8 weeks and the other $3.7 \times 10^{15}/l$ over 5 months. Both female patients had normal thyroid function tests and the male patients were all clinically euthyroid. Vitamin B12 and folate levels were available for 12 patients who had been sampled when the MCV was noted to be elevated and were normal. All the patients were on prophylaxis for *Pneumocystis carinii* pneumonia (cotrimoxazole, dapsone, or pentamidine) for at least 6 months before starting stavudine and therapy had not been changed in any patient. Apart from these drugs none of the patients was taking any other drugs which are associated with macrocytosis. Eight patients discontinued zidovudine at the point of starting stavudine; in each case the MCV increased where it might have been expected to fall. One patient who was prescribed stavudine did not develop macrocytosis. He was challenged regarding his compliance and admitted to never having taken the drug.

The results are summarised in the table. There is a progressive increase in MCV with the duration of treatment. As this was a retrospective study, MCV values for certain periods were not available for all the patients and some patients have not yet completed 20 weeks on stavudine.

To the best of our knowledge, macrocytosis has not been reported in association with stavudine until we notified the Committee on Safety of Medicines. The mechanism of zidovudine induced macrocytosis is unknown. Since both these drugs are thymidine analogues and are known to share metabolic pathways, the mechanisms may be similar.

SAMEENA AHMAD
ASHISH SUKTHANKAR
University Hospital NHS Trust,
Birmingham

Accepted for publication 15 July 1997

Biopsy of male genital dermatoses

In 1993 a paper was published in *Genitourinary Medicine* on the experience of genitourinary physicians in the diagnosis of penile dermatoses and the usefulness of penile biopsy.¹ Of 71 patients seen over a 1 year period, 60 (85%) underwent a penile biopsy as the diagnosis was not made on clinical grounds. A clinical diagnosis was made in nine patients and penile biopsy considered unnecessary. Histological findings were consistent with the initial clinical diagnosis in 33% of the 60 patients undergoing a biopsy and it was concluded that diagnosis based on clinical appearance alone is inadequate. We would like to report our experience on the use of penile biopsy within the setting of a special penile dermatoses clinic in the dermatology department in which the patients were assessed by a dermatologist with an interest in dermatoses of the male genitalia.

A specific monthly clinic was set up in the dermatology department in 1993 for the diagnosis and management of men with penile dermatoses. Patients are referred to the clinic from various sources including the genitourinary clinic, the general dermatology clinic, dermatologists from other hospitals, and general practitioners. The clinic is run by a dermatologist with an interest in diseases of the male genitalia (CB) and attended by a genitourinary physician (DH) and, more recently, a urologist (MD).

In all, 286 patients have been assessed over a 4 year period. Patients ranged in age between 18 and 93 years with the exception of two patients who were 4 and 12 years old. The majority of patients ($n = 223$) ranged in age between 18 and 50 years. The commonest presenting conditions were psoriasis ($n = 68$), penile infections ($n = 47$), seborrhoeic dermatitis ($n = 26$), lichen sclerosis ($n = 36$), lichen planus ($n = 28$), Zoon's balanitis ($n = 23$), and eczema ($n = 21$). Less common diagnoses were vitiligo ($n = 7$), irritant contact dermatitis ($n = 9$), lichen simplex ($n = 6$), allergic contact dermatitis ($n = 3$), Bowen's disease ($n = 3$), Bowenoid papulosis ($n = 3$), squamous cell carcinoma ($n = 1$) and balanoposthitis ($n = 2$), idiopathic penile oedema ($n = 2$), and circinate balanitis ($n = 1$).

In most cases ($n = 218$, 77%) a clinical diagnosis was reached without the need for a penile biopsy. A total of 65 patients (23%) were biopsied: 19/36 (53%) patients with lichen sclerosis were biopsied of whom six (32%) had a biopsy performed to elucidate the diagnosis as a firm diagnosis could not be made on clinical grounds; 13 patients with lichen sclerosis (68%) had a biopsy performed to confirm the clinical diagnosis and assist clinical management; 17/23 (74%) of patients with Zoon's balanitis were biopsied, in all cases to confirm the clinical diagnosis, two patients with a clinical diagnosis of Zoon's balanitis and lichen sclerosis had dual pathology confirmed histologically; 10/28 (36%) patients with lichen planus

were biopsied, of these four (40%) were biopsied to elucidate the diagnosis because of clinical uncertainty, while six were biopsied to confirm the clinical diagnosis; 5/21 (24%) patients with eczema, 4/30 (13%) patients with viral warts, 2/68 (3%) of patients with psoriasis were biopsied, in each case to confirm the clinical diagnosis. All patients with Bowen's disease ($n = 3$), Bowenoid papulosis ($n = 3$), and the case of squamous cell carcinoma had a penile biopsy to confirm the diagnosis and inform the clinical debate about management. A clinical diagnosis without the need for biopsy was made in all cases of seborrhoeic dermatitis, lichen simplex, allergic contact dermatitis, idiopathic oedema, vitiligo, and in the case of circinate balanitis.

There was a very high concordance between clinical diagnosis and histological diagnosis and in only two cases did the findings result in a change in the diagnosis. In both of these a clinical diagnosis of lichen sclerosis was made while in one features of lichen planus were present histologically and in the other the histological findings were non-specific.

In our experience most patients with inflammatory penile disease such as psoriasis, eczema, lichen simplex, contact dermatitis, and lichen planus have cutaneous signs at extragenital sites and a full examination enables a firm diagnosis which may obviate the need for biopsy. The presence of extragenital cutaneous inflammatory skin disease helps to corroborate the diagnosis.

Most dermatoses of the male genitalia are amenable to clinical diagnosis reached on classic dermatological grounds of full history taking and complete physical examination. Penile biopsies do not need to be performed routinely although they may be useful in confirming the clinical diagnosis. Secondly, a histological diagnosis may be valuable in advancing patient management—for example, increasing the authority with which surgery is advocated in diseases such as lichen sclerosis and Zoon's balanitis where circumcision may be necessary.

E MALLON
J S ROSS

Department of Dermatology
D A HAWKINS

Department of Genitourinary Medicine
M DINNEEN

Department of Urology
N FRANCIS

Department of Histopathology
C B BUNKER

Department of Dermatology,
Chelsea and Westminster Hospital,
London SW10 9NH

1 Hillman RJ, Walker MM, Harris JRW, Taylor-Robinson D. Penile dermatoses: a clinical and histopathological study. *Genitourin Med* 1993;68:166-9.

Accepted for publication 15 July 1997

Characterisation of high level tetracycline resistant *Neisseria gonorrhoeae* isolates

Three of 1039 clinical isolates from consecutive patients with urethritis, who attended urological or STD clinics in Tokyo and Kanagawa area between 1985 and 1995, were determined as tetracycline resistant *Neisseria gonorrhoeae* (TRNG). These strains had minimum inhibitory concentrations (MICs) of ≥ 16 mg/l and gave a zone of inhibition of < 30 mm from the edge of the 30 μ g tetracy-

Progressive increase in MCV related to duration of treatment with stavudine

Time	No of patients	Median MCV ($\times 10^{15}/l$)	Mean increase in MCV ($\times 10^{15}/l$)	95% CI
0	17	95.60	—	—
0-4 weeks	13	97.10	3.95	1.15, 6.76
4-8 weeks	14	102.00	4.71	0.37, 9.04
8-12 weeks	9	98.90	8.41	0.89, 15.99
12-20 weeks	7	105.05	10.47	4.10, 16.84
>20 weeks	7	112.00	12.44	6.47, 18.42